

REMARKS

As an preliminary matter, Applicant respectfully requests that the Attorney Docket No. be changed from 106941.181 to 8449-156-999 to reflect the change indicated on the Revocation and Power of Attorney filed on March 11, 2004.

Claims 19, 21-28, 63-78, 90, 92-103, 105-114, and 127-128 were pending in the present application. Claims 113 and 127 have been canceled without prejudice, to expedite prosecution and also since the recited methods are already covered by the broader claims upon which these claims depended. Applicant reserves the right to prosecute the subject matter of the canceled claims in one or more related applications. Claims 114 and 128 have been amended to correct dependency in view of the canceled claims.

Claims 19, 63, 65, 69, 71, 73, 75, and 109 have been amended to clarify that which Applicant regards as the invention. Specifically, claims 19, 63, 65, 69, 71, 73, and 75 have been amended to recite that the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect. Support for these amendments can be found in the specification, for example, at page 14, lines 4-6. These amendments are made without prejudice, solely to expedite prosecution.

Claim 109 has been amended to recite that the immunostimulatory oligonucleotide comprises "at least one chemical group" instead of "one or more chemical groups." Support for this amendment can be found in the specification, for example, at page 9, line 14 to page 10, line 9.

Claim 92 has been amended to correct an improper dependency. Claim 103 has been amended to correct a typographical error.

Claims 22, 23, 63, 92, 93, 94, 105, 106, and 107 have been amended to improve clarity. Support for these amendments can be found in the specification, for example, at page 11, lines 6-10.

Claims 24-26, 28 and 78 have been amended to also be dependent upon claim 23. Claim 112 has been amended to also be dependent upon claim 107. New claims 150-161 are all dependent claims that have been added to recite specific embodiments wherein

1. the saponin is a substantially pure saponin;
2. the saponin is a substantially pure saponin and the saponin is QS-21;
3. the saponin is chemically modified;

4. the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCCTGACGTT (SEQ ID NO:2);

5. the immunostimulatory oligonucleotide comprises at least one chemical group selected from the group consisting of phosphorothioate, alkylphosphonate, phosphorodithioate, alkylphosphorothioate, phosphoramidate, 2-O-methyl, carbamate, acetamidate, carboxymethyl ester, carbonate, and phosphate triester; and

certain combinations thereof. Support for these amendments can be found in the specification, for example, at page 9, line 14 to page 10, line 10, and at page 11, line 1 to page 12, line 7.

No new matter has been added by these amendments. Upon entry of these amendments, claims 19, 21-28, 63-78, 90, 92-103, 105-112, 114, 128, and 150-161 will be pending in the present application.

Applicant respectfully requests that the amendments and remarks made herein be entered and fully considered.

INTERVIEW SUMMARY RECORD

Applicant and Applicant's representatives wish to thank Primary Examiner Michael C. Wilson for the courtesy of the telephonic interview of June 28, 2005 with Applicant's representatives, Adriane M. Antler and Henry P. Wu, in connection with the above-referenced application.

During the Interview, the status of claims 103 and 105-112 was discussed. Dr. Antler pointed out that the first sentence of the section entitled "Claim Rejections - 35 USC 112" was inconsistent with the rejections set forth. Specifically, the first sentence stated that claims 64, 67, 68, 70, 72, 74, 76, 90, 92-103, 105-114, 127 and 128 remain rejected. However, the only remaining rejection under 35 U.S.C. § 112, first paragraph was directed to claims 113 and 127. The Examiner suggested that Applicant point out that the rejection of claim 103 was withdrawn and that, therefore, claim 103 and claims dependent therefrom, i.e., claims 105-112, are not part of the pending rejection.

The claim rejections under 35 U.S.C. § 103 were also discussed. Dr. Antler suggested adding the phrase "wherein the immunostimulatory oligonucleotide and the saponin adjuvant have a synergistic adjuvant effect" to the claims and pointed out that support could be found in the specification on page 14, lines 4-6. Examiner Wilson suggested making the change in

hopes of expediting prosecution and stated that the amendment “might work” to overcome the rejection.

I. Claim Objections

The Examiner alleges that the term “groups” in claim 109 should be “group.” Applicant respectfully disagrees. However, in an effort to advance prosecution of the present application, Applicant has amended claim 109 to recite “at least one group.” Thus, the claim objection has been obviated.

II. Rejections Under 35 U.S.C. § 112

A. The Rejections Under 35 U.S.C. § 112, first paragraph

Applicant notes that the rejection of claims 64, 67, 68, 70, 72, 74, 76, 90 and 103 under 35 U.S.C. 112, first paragraph has been withdrawn.

Claims 113 and 127 are the only claims that remain rejected under 35 U.S.C. § 112, first paragraph. Claims 113 and 127 allegedly contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Without admitting to the propriety of the rejection and in an effort to advance prosecution of the present application, Applicant has canceled claims 113 and 127. Thus, the rejection has been obviated. Accordingly, Applicant respectfully requests withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

III. Rejections Under 35 U.S.C. § 103

Claims 19, 21-27, 63-68, 73-77, 90, 95-98, 100-102, 113, 114, 127 and 128 remain rejected or are rejected under 35 U.S.C. § 103(a) as being unpatentable over Weiner *et al.*, 1997, *Proc. Natl. Acad. Sci. USA* 94:10833-10837 (“Weiner”) in view of Kensil, 1996, *Critical Reviews in Therapeutic Drug Carrier Systems* 13:1-55 (“Kensil”) (Office Action, paragraph III). Claims 19, 21, 24, 25, 27, 28, 65, 67, 69, 70, 73-77, 90, 95-98, 100-102, 113, 114, 127 and 128 remain rejected or are rejected under 35 U.S.C. § 103(a) as being unpatentable over Weiner in view of Kensil (Office Action, paragraph IV). Claims 19, 21-27, 63-68, 71-78, 90, 95-98, 100-102, 113, 114, 127 and 128 remain rejected or are rejected under 35 U.S.C. § 103(a) as being unpatentable over Chu *et al.*, 1997, *J. of Exp. Med.* 186:1623-1631 (“Chu”) in view of Kensil (Office Action, paragraph V). Applicant respectfully disagrees.

As an initial matter, Applicant notes that claims 92-94 and 99, which recite that the saponin comprises a substantially pure saponin or that the immunostimulatory oligonucleotide comprises TCTCCCAGCGTGCGCCAT (SEQ ID NO:1) or TCCATGACGTTCTGACGTT (SEQ ID NO:2), were not rejected under 35 U.S.C. § 103 (or for any other reason set forth in the Office Action).

The Examiner contends that it would have been obvious to combine the two known adjuvants (oligonucleotide 1643 with QS-7, -17, -18, or -21; oligonucleotide 1758 with Quil A; or oligonucleotides 1826 or 1760 with Quil A, QS-7, -17, -18, or -21). The Examiner contends that one of ordinary skill in the art would have recognized that (1) Weiner or Chu in combination with Kensil are both directed towards compositions with adjuvants that increased an immune response; and (2) it was common to combine adjuvants to increase an immune response. The Examiner further contends that one of ordinary skill in the art would have been motivated to combine an immunostimulatory oligonucleotide and saponin to increase an immune response.

At the suggestion of the Examiner and in an effort to expedite prosecution of the present application, Applicant has amended claims 19, 63, 65, 69, 71, 73, and 75 to recite “wherein the saponin and immunostimulatory oligonucleotide have a synergistic adjuvant effect.”

As amended, claims 19, 63, 65, 69, 71, 73, and 75 require that the saponin and immunostimulatory oligonucleotide have a synergistic effect. Thus, the unexpected results are a requirement of the claims and are representative of the genus claimed. Accordingly, Applicant respectfully submits that the unexpected result of synergism of CpG oligonucleotides and *Quillaja saponaria* (QS) saponins as specified by the claims rebuts any *prima facie* case of obviousness.

With respect to CpG oligonucleotides acting in the same manner, Applicant respectfully reiterates her position that the unexpected results seen with every oligonucleotide tested, i.e., CpG 1758, 1826 and 2006, are representative of the genus of CpG oligonucleotides. Variation with concentration is an expected common dose response effect, and does not negate this conclusion.

With respect to QS-21 representing the genus of QS saponins, the Examiner contends that since QS-21 shows adjuvant activity at some concentrations, but not others, one of ordinary skill in the art could not reasonably conclude that QS-21 would exhibit synergy in any immune activity and that such synergy would occur at any concentration. Applicant respectfully reiterates her position that the unexpected results seen with QS-21 is

representative of the genus of QS saponins. Variation with concentration is an expected common dose response effect, and does not negate this conclusion.

Nevertheless, the claims have been amended to specify that the synergistic adjuvant activity is displayed by the immunostimulatory oligonucleotide and saponin of the claims.


In view of the foregoing, Applicant respectfully requests that the Examiner withdraw the rejections under 35 U.S.C. § 103.

CONCLUSION

Applicant respectfully requests that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and a notice of allowance are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Date: August 2, 2005

Respectfully submitted,


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Enclosures